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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,842	01/23/2002	Nicholas W. Gale	REG 900A	7875

7590 04/21/2003

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EXAMINER
JONES, DAMERON

ART UNIT	PAPER NUMBER
1616	7

DATE MAILED: 04/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/055,842	GALE ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2002 and 01 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of Paper No. 4, filed 4/30/02, wherein the specification was amended.

Note: Claims 1-42 are pending.

RESPONSE TO APPLCIANT'S ELECTION

2. The Examiner acknowledges Applicant's election of Group II, in Paper No. 6, filed 4/01/03. The Examiner has found Applicant's arguments persuasive; thus, the restriction requirement is withdrawn.

112 REJECTIONS

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims as written are confusing because it is unclear whether Applicant actually intended the 'capable of …' phrases to be positive limitations in the claims. For example, in claim 1, line 3, the phrase 'molecule capable of detecting ephrin-B2' is disclosed. Did Applicant intend the phrase to be 'molecule detects ephrin-B2'? The expressions are different since in the first expression, the phrase is not read as a positive limitation in the claim. Applicant is reminded that the recitation that an element is 'capable of' performing a function is not a positive limitation, but only requires the

ability to so perform that function. Thus, the expression does not constitute a limitation in any patentable sense (*In re Hutchison, 69 USPQ 138*). Hence, Applicant is respectfully requested to make the appropriate corrections, if necessary, in order that one may readily determine what is being claimed.

103 REJECTION

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-9 and 11-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al (US 2002/0136726 A1).

Anderson et al disclose artery smooth muscle and vein smooth muscle specific proteins and their uses which involve the use of a transmembrane ligand, ephrin-B2 (see entire document, especially, abstract). In addition, Anderson et al disclose (a) once embodiment involves an oligonucleotide encoding a targeting molecule wherein the targeting molecule is composed of a nucleic acid which encodes a promoter and/or enhancer region and a second nucleic acid which encodes a polypeptide targeted to the arteries. The targeting molecules may be administered to a mammal to modulate (e.g., inhibiting) angiogenesis (page 2, paragraph [0011]; page 8, paragraph [0060] – [0061]; page 8, paragraph [0063]). (b) Another embodiment relates to a method of modulating angiogenesis (e.g., inhibiting or promoting) or inhibiting tumor growth in a mammal

(page 22, paragraph [0013]; page 13, paragraph [0092]). (c) The terms ephrin and Eph refer to ligands and receptors, respectively that can be used from any animals (e.g., mammals/non-mammals, vertebrates/non-vertebrates, including humans) (page 4, paragraph [0027[). (d) Another embodiment involves testing an effect of an agent (e.g., a drug, a nucleic acid, a gene product, or a targeting molecule) on growth, development, recruitment, and/or proliferation of arties. The method may be administered to a subject having a tumor (page 5, paragraph [0043]; page 7, paragraph [0056]). (e) Possible screening approaches include screening for angiogenic effects, anti-angiogenic effects, anti-thrombotic effects, anti-stenotic and/or anti-restenotic effects, inhibition of formation of atherosclerotic plaques, and effects of vasotension (page 8, paragraph [0063]; pages 8-9, paragraph [0065]). (f) The ephrin compositions may comprise a label which may be a radioactive isotope, a fluorescent label, a colorimetric label, an enzyme label, an affinity label, and epitope label, and a chemiluminescent label (page 9, paragraph [0068]). (g) The targeting agents may be an imaging agent (page 10, paragraph [0077]; page 11, paragraph [0079]). (h) Targeting vehicles may be administered using parenteral, oral, transdermal, topical or rectal administration (page 11, paragraph [0081]). (i) Antibodies e.g., polyclonal or monoclonal antibodies) may be conjugated to ephrin-B2 (page 12, paragraph [0085]. (j) The extracellular domain of the ephrin family ligand or the extracellular domain of an Eph family receptor is fused to the Fc domain of human immunoglobin (page 12, paragraph [0086]; page 17, Example 13). Anderson et al fail to disclose a kit comprising the ephrin-B2 compositions and specifically state that the composition may for vascular cell death.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Anderson et al and use the ephrin-B2 composition for imaging tumors, causing vascular cell death, delivering an agent to the vasculature, and generating a kit comprising the ephrin-B2 composition because: (1) Anderson et al disclose imaging tumors and delivering an agent to the vasculature (see discussion above). In addition, it would be obvious to use the composition for causing vascular cell death because a skilled practitioner in the art would recognize that if you inhibit tumor growth by administering an ephrin-B2 compositions, then cell death is occurring since the tumor's growth is inhibited. In regards to generating a kit comprising the composition components, it would be obvious to one of ordinary skill in the art at the time the invention was made to generate a kit for diagnostic and therapeutic purposes because of the ever present need for such kits in hospitals, clinics, or other medical facilities. In addition, a skilled artisan would be capable of putting the various components of the composition in packages to be later mixed and used in such facilities.

COMMENTS/NOTES

7. It should be noted that no prior art has been cited against claim 10. However, Applicant must address and overcome the 112, second paragraph, rejection as it relates to claim 10.

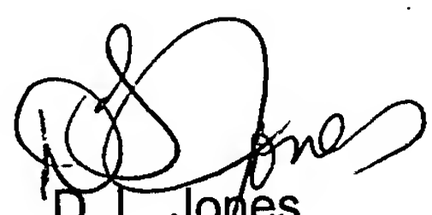
Note: Claim 10 is allowable over the prior art of record because the prior art neither anticipates nor renders obvious a method of causing vascular endothelial cell death by targeting tumor vasculature comprising administering to a subject a

composition comprising a ephrin-B2 nucleic acid or polypeptide coupled to carboplatin, cisplatin, vincristine, methotrexate, paclitaxel, docetaxel, 5-fluorouracil, UFT, hydroxyurea, gemcitabine, vinorelbine, irinotecan, tirapazamine, or matrilysin.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (703) 308-4640. The examiner can normally be reached on Mon.-Fri. (alternate Mon.), 6:45 a.m. - 4:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose' Dees can be reached on (703) 308- 4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



D. L. Jones
Primary Examiner
Art Unit 1616

April 17, 2003